

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
15 April 2004 (15.04.2004)

PCT

(10) International Publication Number  
**WO 2004/031774 A3**

(51) International Patent Classification<sup>7</sup>: **G01N 33/574**,  
C07K 16/30, C12Q 1/68, A61K 39/00, C07K 14/47,  
A61P 35/04

(21) International Application Number:  
PCT/JP2003/010338

(22) International Filing Date: 14 August 2003 (14.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/414,709 30 September 2002 (30.09.2002) US

(71) Applicants (for all designated States except US): **ON-COTHERAPY SCIENCE, INC.** [JP/JP]; 3-16-13, Shirokanedai, Minato-ku, Tokyo 108-0071 (JP). **JAPAN AS REPRESENTED BY THE PRESIDENT OF THE UNIVERSITY OF TOKYO** [JP/JP]; 3-1, Hongo 7-chome, Bunkyo-ku, Tokyo 113-8654 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **NAKAMURA, Yusuke** [JP/JP]; 17-33, Azamino 1-chome, Aoba-ku, Yokohama-shi, Kanagawa 225-0011 (JP). **FURUKAWA, Yoichi** [JP/JP]; 10-40, Miyazaki 3-chome, Miyamae-ku, Kawasaki-shi, Kanagawa 216-0033 (JP).

(74) Agents: **SHIMIZU, Hatsushi et al.**; Kantetsu Tsukuba Bldg. 6F, 1-1-1, Oroshi-machi, Tsuchiura-shi, Ibaraki 300-0847 (JP).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
14 October 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR TREATING OR PREVENTING METASTASIS OF COLORECTAL CANCERS

(57) Abstract: Disclosed are methods of detecting metastasis of colorectal cancer using differentially expressed genes. Also disclosed are methods of identifying agents for treating colorectal cancer or preventing metastasis of colorectal cancer.



WO 2004/031774 A3

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/10338

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/574 C12Q1/68 C07K14/47 C07K16/30 A61K39/00  
A61P35/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEEPER DANIEL S ET AL: "A functional screen identifies hDRIL1 as an oncogene that rescues RAS-induced senescence" NATURE CELL BIOLOGY, vol. 4, no. 2, February 2002 (2002-02), pages 148-153, XP002273791 ISSN: 1465-7392 abstract  ----- -/-	1-8, 10-14, 20,26

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

17 March 2004

Date of mailing of the international search report

17. 03. 04

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Lopez García, F

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/JP 03/10338

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>YANAGAWA R ET AL: "GENOME-WIDE SCREENING OF GENES SHOWING ALTERED EXPRESSION IN LIVER METASTASES OF HUMAN COLORECTAL CANCERS BY CDNA MICROARRAY" NEOPLASIA, DOYMA, BARCELONA,, ES, vol. 3, no. 5, September 2001 (2001-09), pages 395-401, XP009024057 ISSN: 0212-9787 cited in the application abstract</p>	1-8, 10-14, 20,26
X	<p>YANAGAWA R ET AL: "IDENTIFICATION OF GENES ASSOCIATED WITH LIVER METASTASIS OF COLORECTAL CANCER BY MEANS OF CDNA MICROARRAY" PROCEEDINGS OF THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW YORK, NY, US, vol. 42, 24 March 2001 (2001-03-24), page 59, XP001157334 ISSN: 0197-016X the whole document</p>	1-8, 10-14, 20,26
X	<p>WO 02/21996 A (EOS BIOTECHNOLOGY INC ;GISH KURT C (US); MACK DAVID H (US); WILSON) 21 March 2002 (2002-03-21) Paragraph 6, 7, 24, 25; Tables 1, 2; Claims 1-31.</p>	1-8, 10-14, 20,26
X	<p>SUZUKI MITSUHIRO ET AL: "A novel E2F binding protein and Myc-type HLH motif stimulates E2F-dependent transcription for forming a heterodimer" ONCOGENE, vol. 17, no. 7, 20 August 1998 (1998-08-20), pages 853-865, XP002273792 ISSN: 0950-9232 abstract</p>	26
P,X	<p>WO 03/029273 A (WHITEHEAD BIOMEDICAL INST ;STAUNTON JANE (US); GOLUB TODD (US); BH) 10 April 2003 (2003-04-10) p. 95, ID No. 103.</p>	1-8, 10-14, 20,26
T	<p>LI M ET AL: "GENES ASSOCIATED WITH LIVER METASTASIS OF COLON CANCER, IDENTIFIED BY GENOME-WIDE CDNA MICROARRAY" INTERNATIONAL JOURNAL OF ONCOLOGY, EDITORIAL ACADEMY OF THE INTERNATIONAL JOURNAL OF ONCOLOGY,, GR, vol. 24, no. 2, February 2004 (2004-02), pages 305-312, XP009027443 ISSN: 1019-6439 the whole document</p>	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/10338

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0221996	A	21-03-2002	US 2003077568 A1	24-04-2003
			AU 9090201 A	26-03-2002
			CA 2422278 A1	21-03-2002
			EP 1317669 A2	11-06-2003
			JP 2004515225 T	27-05-2004
			WO 0221996 A2	21-03-2002
			US 2002102544 A1	01-08-2002
WO 03029273	A	10-04-2003	WO 03029273 A2	10-04-2003
			US 2004009489 A1	15-01-2004

# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/JP 03/10338

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 9  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 15  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-8, 10-14, 20, 26 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 1-8 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 17-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

-----  
Continuation of Box I.1

Claims Nos.: 9

Claims 1-8: Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

Claim 9: Rule 39.1(v) PCT - Presentation of information

Claims 17-22: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

-----  
Continuation of Box I.2

Claims Nos.: 15

Present claims 15 refers to reagents that bind to the nucleic acids MLXs 1-163 without giving a true technical characterization. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is not found in the application. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, no search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

Present claims 17 and 23 refer to methods of treatment using "compounds obtained by the methods according to any of the claims 1-5" and to compositions comprising the "compounds obtained by the methods according to any of the claims 1-5" without giving a true technical characterization. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is not found in the application. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, no search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

Present claims 21-22 which do not contain any technical feature to

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

characterize a "method for inducing an anti-tumor immunity" so lack clarity (Art. 6 PCT) and support in the description (Art. 5 PCT) that no meaningful search can be carried out (Art. 6 PCT).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.